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10/530,728	04/08/2005	James Landers	119620.00112	9332

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EXAMINER	
HOBBS, MICHAEL L	

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4151	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/530,728	LANDERS, JAMES	
	Examiner	**Art Unit**	
	MICHAEL L. HOBBS	4151	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE _3_ MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on _08 April 2005_.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) _1-38_ is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) _1-38_ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on _08 April 2005_ is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _04/08/2005_.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Specification

1. The specification is objected to as failing to provide proper antecedent basis for the claimed subject matter. See 37 CFR 1.75(d)(1) and MPEP § 608.01(o). Correction of the following is required: in claim 18 starting on line1, applicant refers to the IR source is "disposed in a spaced relationship..." where "spaced relationship” does not appear in the specification. Furthermore, the applicant in claim 26 line 2 states that the waveguide will “conduct radiation from the non-contact heating source" where the phrase "conduct radiation" does not appear in the specification. The examiner's assumption is that the applicant meant "deliver radiation” as is stated on page 22 line 11 of the specification.

Claim Objections

2. Claim 11 is objected to because of the following informalities: on line 1 of the claim applicant refers to the “interferometer is and…” where the "and" is a misspelling and that “an” was meant in the phrase. Appropriate correction is required.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-6, 8, 9, 12-19, 21, 26-31 and 33 are rejected under 35 U.S.C. 102(b) as being anticipated by Landers et al. (U.S. 6,210,882).

5. Landers teaches a rapid thermocycling method that uses non-contact heating and cooling means to control the temperature of the samples. For claim 1, Landers teaches a microchip with micro-chambers (Abstract) that are heated with a non-contact heating source (Abstract). In claim 2, Landers discloses a non-contact cooling means for cooling such as directing an air stream to cool the vessel such as forcing the air across the vessel (col. 10 lines 61-62). Also, for claim 3 Landers teaches that the air source is compressed air which results in more rapid cooling than by heat dissipation alone (col. 10 lines 62-63). With regards to claim 4, Landers teaches that the temperature of the compressed air can be adjusted to affect the cooling rate (col. 14 lines 64-65, col. 15 lines 7-8) implying that the compressor chills the air sent to the microchip. Landers for claim 5 teaches that the pressure for the air source can be adjusted between 1 and 150 psi (col. 26 lines 61-63) and for claim 6 that a solenoid valve can be used to regulate the flow of compressed air (col. 14 lines 65-66). Regarding claim 8, Landers teaches that the temperature is monitored (col. 13 lines 58-59) such as a thermocouple (col. 15 lines 18-20). With regards to claim 9, Landers teaches that the temperature monitoring means is either a thermocouple (Col. 15 lines 28-30) or a remote temperature sensing means such as a thermo-optical sensing device (col. 15 lines 39-41). Also, for claim 12, Landers teaches that a microprocessor monitors and regulates the temperature through feed back from a thermocouple, for example (col. 15 lines 13-14) where the microprocessor/computer controls the heating

and cooling means by using switches and/or valves (col. 15 lines 45-47) with control of the microchip being inherent in the set-up of the micro-chip. With regard to the plurality of temperatures and dwell times of claim 13, Landers teaches that the thermocycler operates at several desired temperatures such as 94, 54 and 72 ^{o}C and dwell times of 30 sec./30 sec./ 60 sec. and 2 sec./2 sec./4 sec. respectively (Fig. 7A-7D) and can have as many heating steps as necessary (col. 10 lines 56-57). With regards to claim 14, Landers teaches performing DNA amplification (col.1 lines 54-56) through a PCR mediated amplification of the l DNA sequence (Figs. 11A and 11B). For claim 15, the non-contact heating source is an IR source (col. 26 lines 53-54). For claims 16 and 17, the IR source is a halogen lamp (col. 26 lines 55-56) and a tungsten lamp (col. 26 lines 57-58). For claim 18, Landers teaches that a window in the microchip allows the IR source to directly heat the sample contained within (co. 9 lines 24-26, Fig. 1A element 12). Furthermore, the phrase **in a spaced relationship with** is being interpreted to mean that the IR source is not within the reaction chamber of the microchip. With this interpretation, the IR source of Landers is in a spaced relationship with the microchip.

6. For claim 19, Landers teaches a filter between the IR source and the microchip (col. 16 line 53, Fig. 6A element 168). With regards to claim 21, Landers teaches that a sample reservoir (Fig. 1D element 8) is connected to a main micro-channel (Fig. 1D element 12) connected to a waster reservoir (Fig. 1D element 10). Both reservoirs are connected to the main micro-channel via a second and third micro-channel respectively (col. 9 lines 42-43 & 46-48, Fig. 1D elements 20 & 22) where the reservoirs and micro-channels are in communication with an outlet reservoir (col. 9 line 66-67, col. 10 line 1).

With regards to claim 26, Landers teaches a window that is in the glass upper window (col. 9 lines 24-26, Fig. 1 element 12) that allows IR light wavelengths to heat the PCR chamber (col. 9 lines 50-51). Furthermore, the window can also be made of plastic or any other transparent material (col. 9 line 51).

7. For claim 27, Landers teaches providing a microchip (Abstract) with micro-chambers (Abstract, col. 8 lines 62-63) while placing a volume of the sample in the nano-liter range into the reaction vessel (col. 25 lines 66-67). Also, Landers teaches heating the sample with the non-contact heating source (col. 26 lines 1-2), cooling the sample with the non-contact cooling source (col. 26 lines 6-7) and sequentially repeating the heating and cooling steps to perform a desired number of thermocycles (col. 26 lines 11-12). For claim 28, Landers teaches the step where the non-contact heating source is an IR lamp (col. 26 liens 53-54). Regarding claims 29 and 30, Landers teaches using an IR source that is a halogen lamp (col. 26 lines 55-56) or a tungsten lamp (col. 26 lines 57-58). For claim 31, Landers teaches the step where a window in the microchip allows the IR source to directly heat the sample contained within (co. 9 lines 24-26, Fig. 1A element 12). Furthermore, the phrase **in a spaced relationship with** is being interpreted to mean that the IR source is not within the reaction chamber of the microchip. With this interpretation, the IR source of Landers is in a spaced relationship with the microchip. For claim 33, Landers teaches the step where a sample reservoir (Fig. 1D element 8) is connected to a main micro-channel (Fig. 1D element 12) connected to a waster reservoir (Fig. 1D element 10). Both reservoirs are connected to the main micro-channel via a second and third micro-

channel respectively (col. 9 lines 42-43 & 46-48, Fig. 1D elements 20 & 22) and it is inherent that the reservoirs and channels are fluidly connected. Therefore, Landers meets the limitations of claims 1-6, 8, 9, 12-19, 21, 26-31 and 33.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. The factual inquiries set forth in *Graham* **v.** *John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

10. Claims 23, 24, 25 and 35-38 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers et al. (U.S. 6,210,882) in view of Kelln et al. (U.S. 4,738,825).

11. Landers is silent regarding the limitations of claims 23-25 and 35-38.

12. Kelln teaches a cuvette handling system that includes a multi-cuvette unit supply station, a loading station and an analysis station. Specifically, Kelln teaches analyzing individual cuvettes on a rotor with an optical testing device that examines the extent of

reaction within each vessel. For claim 23, Kelln teaches that a plurality of spaced elongated chamber cuvettes are arranged in a circumferential array (col. 1 lines 14-16) and for claim 24 the cuvettes are mounted on a rotor (col. 1 line 16). With regards to claim 25, Landers and Kelln do not specify that the cuvettes are equidistant from the center of the rotor, but based on Fig 2 of Kelln, the cuvettes are arranged equidistant from the center of the rotor. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the rotor as suggested by Kelln within the teachings of Landers in order to index from one cuvette to another in order to analyze the sample in each cuvette. The suggestion for doing so at the time would have been in order to keep track of each sample and automate testing and data collection for a large number of samples.

13. For claim 35, Kelln teaches the step where a plurality of spaced elongated chamber cuvettes are arranged in a circumferential array (col. 1 lines 14-16) and for claim 36, Kelln mounts the cuvettes on a rotor (col. 1 line 16). With regards to claim 37, Kelln does not specify the step in which the cuvettes are equidistant from the center of the rotor, but based on Fig 2 of Kelln, the cuvettes on each row are arranged equidistant from the center of the rotor when compared to the cuvettes on the same row. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the rotor as suggested by Kelln within the teachings of Landers in order to index from one cuvette to another in order to analyze the sample in each cuvette. The suggestion for doing so at the time would have been in order to keep track of each sample and automate testing and data collection for a large number of samples.

14. Landers teaches a non-contact heating source that relies on an IR source, i.e. halogen or tungsten bulb to heat the surface, but does not specify rotating the microchip to be under the IR source. For claim 38, Kelln does not specify that the cuvettes are heated, but does teach the step of rotating the cuvettes to an analyzer for photometric analysis (col. 4 lines 1-2 & 5, Fig. 2 element 28) which will project a light into the cuvette. This allows each cuvette to be examined individually. Therefore, at the time of the invention, it would have been obvious to one of ordinary skill in the art to employ the method of using a rotor and photometric analysis as suggested by Kelln within the teachings of Landers in order to heat a sample on the rotor. The suggestion for doing so at the time would have been in order to run concurrent reactions and maintain sample identification (col. 1 lines 38-41 of Kelln).

15. Claims 10 and 11 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers et al. (U.S. 6,210,882) in view of Heffelfinger et al. (U.S. 5,885,531).

16. With regards to claim 10, Landers teaches an optical analysis device to analyze the samples, but does not specify that the optical analysis device is an interferometer. Heffelfinger teaches a tunable apparatus that images fluorescence in situ hybridization that uses a common path interferometer as the detection system. For claim 10, Heffelfinger teaches a detection system that is an interferometer (Abstract). Furthermore, for claim 11 the interferometer is a Fabry-Perot etalon as the fluorescence detection system (col. 2 lines 55-56). The Fabry-Perot etalon of Heffelfinger further includes a tunable filter system that can tune to a desired wavelength and also eliminate undesired wavelengths using a band pass filter (col. 6 lines 36-38). Also, the use of a

Fabry-Perot etalon/interferometer is well known in the art (as evidenced by U.S. 3,795,440, U.S. 4,014,614 & U.S. 5,539,517) as part of a spectrometer. Therefore, it would have been obvious to one of ordinary skill in the art to employ the Fabry-Perot interferometer of Heffelfinger within the teachings of Landers in order to image the fluorescence of the cell. The suggestion for doing so would have been in order to visualize DNA sequences in metaphase chromosomes and inter-phase nuclei (col. 3 lines 67 & col. 4 line 1).

17. Claims 22 and 34 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers et al. (U.S. 6,210,882) in view of Wolfgang et al. (DE197 55 479).

18. Landers does not teach the limitations of claims 22 and 34.

19. Wolfgang discloses a PCR reactor that includes a reaction chamber and a wash chamber for the duplication of DNA. For claim 22, Wolfgang teaches that reaction chamber (Fig. 1 element 6) is connected to the cleaning chamber (Fig. 1 element 8) or **reservoir** by a valve (Fig. 1 element 60, page 7 of machine translation lines 27-28). The valve further provides a separation between the reactor and the cleaning chamber and serves to adjust the flow between the chambers due to pneumatic control of the valves and/or pumps (page 3 of translation lines 21-24). At the time of the invention, it would have been obvious to employ the valve as suggested by Wolfgang within the teachings of Landers in order to control the outflow of the sample from the reactor. The suggestion for doing so at the time would have been in order to clean up the amplified DNA before sending the sample to an analysis device (page 3 of translation lines 7-9).

20. For claim 34, Wolfgang teaches the step where the reaction chamber (Fig. 1 element 6) is connected to the cleaning chamber (Fig. 1 element 8) or **reservoir** by a valve (Fig. 1 element 60, page 7 of machine translation lines 27-28). At the time of the invention, it would have been obvious to employ the valve as suggested by Wolfgang within the teachings of Landers in order to control the outflow of the sample from the reactor. The suggestion for doing so at the time would have been in order to clean up the amplified DNA before sending the sample to an analysis device (page 3 of translation lines 7-9).

21. Claim 7 is rejected under 35 U.S.C. 103(a) as being unpatentable over Landers et al. (U.S. 6,210,882).

22. Landers discloses that the forced air is blown over the microchip, but remains silent as to whether the forced air is **angularly offset.** However, one embodiment of Landers discloses cooling jets above the reservoir (Fig. 6C elements 154 & 156) and one cooling jet below and at an angle (col. 16 lines 48-50, Fig. 6C element 156). This has the effect of allowing sharp temperature transitions within the reaction vessel (col. 17 lines 43-44). Therefore, it would be obvious to one of ordinary skill in the art to modify the cooling jets of Landers to an angled jet in order to achieve fast and accurate temperature profiles (col. 17 lines 44-45).

23. Claims 20 and 32 are rejected under 35 U.S.C. 103(a) as being unpatentable over Landers et al. (U.S. 6,210,882) in view of Manz et al. (U.S. 5,599,503).

24. For claim 20, Landers teaches that windows are placed above the micro-heating area to allow non-contact heating (col. 9 lines 24-26, Fig. 1 element 12) where the

windows are integral to the chip. Landers is silent regarding fiber bundles. Manz teaches a detector cell that is designed for measuring small volumes. With regards to claim 20, Manz teaches that the fiber optic light guides are used to send light into the detector cell to measure the sample contained within the micro-channel (col. 3 line 66 and col. 4 lines 1-3). Furthermore, the fiber optic light guides of Manz can be adjusted with regard to light entry and exit where this compensates for refraction effects within the channel (col. 5 liens 39-41). Therefore, it would have been obvious to one of ordinary skill in the art to employ the fiber guides as suggested by Manz within the teachings of Landers in order to send light directly into the microchip. The suggestion for doing so at the time would have been in order to have a reproducible optical path length (col. 3 lines 65-67).

25. For claim 32, Landers teaches the step where windows are placed above the micro-heating area to allow non-contact heating (col. 9 lines 24-26, Fig. 1 element 12) where the windows are integral to the chip. Landers is silent regarding fiber bundles. Manz teaches a detector cell that is designed for measuring small volumes. With regards to claim 32, Manz teaches the step where fiber optic light guides are used to send light into the detector cell to measure the sample contained within the micro-channel (col. 3 line 66 and col. 4 lines 1-3). Furthermore, the fiber optic light guides of Manz can be adjusted with regard to light entry and exit where this compensates for refraction effects within the channel (col. 5 liens 39-41). Therefore, it would have been obvious to one of ordinary skill in the art to employ the fiber guides as suggested by Manz within the teachings of Landers in order to send light directly into the microchip.

The suggestion for doing so at the time would have been in order to have a reproducible optical path length (col. 3 lines 65-67).

Conclusion

26. The prior art made of record and not relied upon is considered pertinent to applicant's disclosure. Corless (WO 98/09728) that teaches a thermal cycling device that includes housing with a heat sink plus an infra-red hating means and a cooling means synchronized with a controller. Also, Murphy et al. (U.S. 5,381,229) teaches an optical interferometer that has a multi-mode sapphire fiber as a high temperature sensor. Furthermore, Cabib et al. (U.S. 5,539,517) teaches using a Fabry-Perot interferometer for the two-dimensional analysis of the spectral intensity of a pixel. Also, Fletcher et al. (U.S. 3,795,448) teaches a Doppler shift system that uses a Fabry-Perot interferometer that measures a particles velocity based on the Doppler shift of the particle and Sandercock teaches a high resolution Fabry-Perot spectrometer.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to MICHAEL L. HOBBS whose telephone number is (571)270-3724. The examiner can normally be reached on Monday-Thursday 7:30 AM - 5:00 PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mikhail Kornnakov can be reached on (571) 272-1303. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

MLH
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